

REMARKS

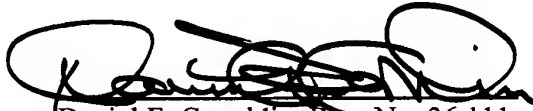
Claims 6-10, 15-20 and new claims 21-23 are present in this application for consideration. Claims 1-5 and 11-15, which were originally filed in the present application, have been canceled, without prejudice. Claims 21-23 have been added by the instant amendment. Support for the added claims can be found in numerous locations in the specification, and in the claims as filed. Thus, no new matter has been added by the instant amendment.

Applicants retain the right to prosecute pre-amended claims at a later date in this application, an application claiming priority from this application, or in any reissue or reexamination application that may be filed in the future, throughout prosecution of the present application.

It is respectfully submitted that the claims under consideration are believed to be patentable over the references of record. Early notification of the allowability of the pending claims is courteously solicited.

Respectfully submitted,

Date: August 25, 2003



Daniel F. Coughlin, Reg. No. 36,111
Edwards & Angell, LLP
Three Stamford Plaza
301 Tresser Blvd., Suite 1310
Stamford, Connecticut 06901
Tel. No. (203) 353-6817

**VERSION WITH MARKINGS TO SHOW CHANGES
MADE TO THE SPECIFICATION**

Please substitute the following paragraph on Page 7 beginning at line 10:

Fig. 2 is a photomicrograph of oncogenic transformed/established tumor cell lines 293GP and ZR-75-1 ~~MCF-7~~ cells cultured in basal medium for twenty-four hours and then treated with Ea-2-, Ea-3, or Ea-4-peptide under control conditions alone, control conditions + α -aminitin, an RNA synthesis inhibitor, or control conditions + cycloheximide, a protein synthesis inhibitor.

Please substitute the following paragraph for the paragraph on Page 7 beginning at line 14:

Fig 3 is a photomicrograph of oncongenic transformed/established tumor cell lines 293GP and MCF-7 ~~ZR-75-1~~ cells cultured under control conditions alone, control conditions +

α -aminitin, an RNA synthesis inhibitor, or control conditions + cycloheximide, a protein synthesis inhibitor ~~in basal medium for twenty four hours and then treated with Ea-2, Ea-3, or Ea-4 peptide.~~

Please substitute the following paragraphs for paragraphs 1 and 2 on page 8:

Fig. 5a is an illustration of a procedure undertaken to transfect a gene construct containing a green fluorescence gene (EGFP) or Ea-4 peptide gene and green fluorescence gene (EGFP) into MDA-MB-231 breast tumor cells, and a method for determining colony formation activity of the transfected Ea-4 positive clones for EGFP controls.

Fig. 5b ~~are~~ and the photomicrographs of MDA-MB-231 breast tumor cells transferred with EGFP alone, and EGFP and Ea-4, with a graph interposed there between that indicates the relative colony formation under each scenario.

Please substitute the following paragraph for the paragraph on Page 12 beginning at line 1:

Results: *Fig. 32* is a photomicrograph of oncogenic transformed/established tumor cell lines 293GP and MCF-7 cells cultured under control conditions alone, control conditions + α -aminitin, an RNA synthesis inhibitor, or control conditions + cycloheximide, a protein synthesis inhibitor. As shown in *Fig. 23*, the morphological changes in the 293GP and MCF-7 cells, induced by the ea-4-peptide, were abolished by treatment with cycloheximide or α -aminitin. The viability of the inhibitor-treated cells

was determined by the dye extrusion assay and the results showed that inhibitor-treated cells remain viable (data not shown). These results from expression of genes that are inactivated during organic transformation or tumor development since these experiments were conducted with oncogenic transformed or established tumor cells. The synthesis of new RNA and proteins appear to be required for the Ea-4-peptide induced morphological changes.

Please substitute the following paragraph for the paragraph on Page 13 beginning at line 3:

Results: Fig. 23 is a photomicrograph of oncogenic transformed/established tumor cell lines 293GP and ZR-75-1 cells cultured in basal medium for twenty-four hours and then treated with Ea-2, Ea-3, or Ea-4 peptide. Although both Ea-2 and Ea-4 peptides are able to induce morphological changes in 293GP or ZR-75-1 cells, the Ea-3 peptide fails to induce any visible morphological change under the identical culture conditions (Figure 4). This observation suggests that the domain of the E-peptide responsible for the induction of morphological changes in the 293GP or ZR-75-1 is not present in the Ea-3-peptide (1).

Please substitute the following paragraph for the paragraph on Page 13 beginning at line 13:

Overview: An obvious change in the characteristics of normal cells after oncogenic transformation is the ~~lost loss~~ of contact inhibition and anchorage-dependent cell division behavior (10). This behavioral change in oncogenic transformed or cancer cells can be easily demonstrated *in vitro* by the colony formation assay in a semi-solid medium (1). Since treatment of oncogenic transformed cells or cancer cells with the Ea-4 peptide results in morphological change and increased cell attachment, it is conceivable that this protection may also affect the anchorage-independent cell division behavior of oncogenic transformed or cancer cells. To test this hypothesis, a colony formation assay was conducted following the methodology described by Yange (9).

Please substitute the following paragraph for the paragraph on Page 15 beginning at line 4:

Methodology: MDA-MB-231 breast tumor cells were transfected with a gene construct containing an Ea-4 peptide gene and a green fluorescence (EGFP) gene and permanent transformants isolated. Both Ea-4-peptide transformants and control cells are subjected to colony formation assay on a soft agar medium and colonies scored. Fig. 5a illustrates the procedure undertaken to transfect the gene construct and the method utilized to determine colony formation of the transfected Ea-4 positive clones as compared to EGFP controls.

Please substitute the following paragraph for the paragraph on Page 15 beginning at line 11:

Results: *Fig. 5b* comprises photomicrographs of MDA-MB-231 breast tumor cells transfected with EGFP alone, and EGFP and Ea-4, with a graph interposed there between that indicates the relative colony formation under each scenario. While numerous colonies are observed in EGFP control cells, no colony was observed in Ea-4-peptide transformed cells.